AMENDMENTS TO THE SPECIFICATION

On page 5, first full paragraph, please replaced the paragraph with the following:

--Figures 1A-1E ~~shows~~ show a comparison of the complete human RIZ amino acid sequence (indicated as hRIZ; SEQ ID NO:4) with the complete rat RIZ amino acid sequence (indicated as rRIZ; SEQ ID NO:2). A consensus sequence is shown. Single letter amino acid symbols are used. Amino acids that are identical in hRIZ and rRIZ are shown as ".". –

On page 20, please replace the paragraph beginning at line 25 with the following:

--*Loss of heterozygosity (LOH) analysis.* Primary normal/tumor pairs were investigated by using fluorescently labeled microsatellites. Primer sequences were obtained from the Genome Database ~~(http://gdbwww.bdb.org/)~~. Amplifications of each microsatellite were done in 15µl volumes with 10 ng of each respective genomic DNA, 8 pmol of each primer (5' primer, fluorescently labeled), 100 µM each dNTP, 0.6 unit of AmpliTaq Gold DNA Polymerase (PE Biosystems, Foster City, CA), 10 mM Tris·HCl (pH 8.3), 50 mM KCl, and 2 mM $MgCl_2$. PCR products were loaded onto a 377XL sequencer (PE Biosystems). Allele size and fluorescent intensity were determined by GENESCAN and GENOTYPER software (PE Biosystems). LOH was analyzed by determining the fluorescent intensity of each allele and calculating the ratio (Canzian et al., Cancer Res. 56:3331-3337 (1996)). A sample was scored as showing LOH if an allelic ratio of <0.67 or >1.5 was obtained.

On page 21, second paragraph, please replace the paragraph beginning at line 14 with the following:

-- Because of a high degree of MSI observed in the HNPCC tumor DNAs, single-nucleotide polymorphisms (SNPs) were also used to determine LOH in the subset of 24

HNPCC normal/tumor DNA pairs. Primer sequences were obtained from the human SNP database ~~(http://www-genome.wi.mit.edu/SNP/human/index.html)~~. SNPs were amplified in 25 μl volumes with 100 nmol of each of the respective PCR primers, 25 ng of genomic DNA, 100 μM each dNTP, 1.0 unit of AmpliTaq Gold DNA Polymerase (Perkin-Elmer), 10 mM Tris·HCl (pH 8.3), 50 mM KCl, and 2 mM $MgCl_2$. PCR products were purified by using exonuclease 1 and shrimp alkaline phosphatase (Amersham Life Sciences) and directly sequenced in one direction with one of the amplification primers and the BigDye Terminator chemistry (PE Biosystems). Samples that failed or sequenced poorly were resequenced in the other direction with the other amplification primer. LOH determination was done by a method similar to the microsatellite analysis.--

On page 24, please replace the paragraph beginning at line 6 with the following paragraph:

-- *Identification of RIZ as a Candidate Gene for 1p Alterations.* Functional candidate genes in the region of 32.2 cM from 1ptel were examined and screened for mutations. The RIZ gene maps to 32.2 cM on GeneMap 99 ~~(http://www.ncbi.nlm.nih.gov/genemap99)~~. RIZ is within 370 kb of D1S228, as inferred from yeast artificial chromosome analysis (Leygue et al., supra (1998)). RIZ lies in 3' to 5' orientation from the telomere of chromosome 1p. In HNPCC tumors, there was a gradual decline of the LOH rate from WIAF-481 to RIZ 3' to RIZ 5'. Three intragenic polymorphisms of RIZ were analyzed for LOH, including a codon Pro-704 deletion at exon 8, an intron 4 CA repeat, and a SNP flanking exon 4 (GAT to GAC 18 bases 3' of the coding exon 4 sequence). The LOH rates for these RIZ markers were 21% (3/14), 9% (1/11), and 0% (0/8), respectively. Tumor 5393T showed LOH of exon 8 Pro-704 but retention of the other intragenic markers, consistent with location of a deletion

break point inside the RIZ gene. Analysis of MSI(-) tumors that were not preselected for 1p LOH revealed LOH rates of 30% (4/13), 23% (3/13), and 60% (3/5), respectively. Tumor 7T-OSU showed LOH of RIZP704 but retention of heterozygosity of RIZ intron 4 CA, again indicating a deletion breakpoint within RIZ. The location of RIZ in the vicinity of the common LOH region and the observed deletion breakpoints within RIZ suggest that RIZ is a candidate target of 1p36 alterations in both hereditary and sporadic colorectal cancers. –